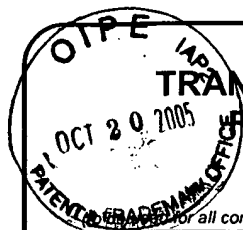


Box 2 of 2

PTO/SB/21 (09-04)



# TRANSMITTAL FORM

For all correspondence after initial filing)

Application Number	09/730,329
Filing Date	December 4, 2000
First Named Inventor	John
Art Unit	1653
Examiner Name	Kam, C.
Attorney Docket Number	015270-006460US
Total Number of Pages in This Submission	17

## ENCLOSURES (Check all that apply)

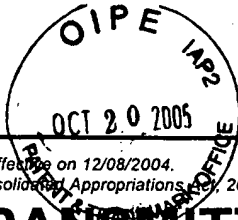
<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Supplemental Information Disclosure Statement (3 pgs.) PTO/SB/08A (5 pgs.) PTO/SB/08B (6 pgs.) <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): 1. Return postcard 2. One Hundred Two (102) references*
Remarks: The Commissioner is authorized to charge any additional fees to Deposit Account 20-1430. * Not included in "Total Number of Pages In This Submission"		

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Townsend and Townsend and Crew LLP		
Signature	<i>Mark G. Sandbaken</i>		
Printed name	Mark G. Sandbaken, Ph.D.		
Date	October 20, 2005	Reg. No.	39,354

## CERTIFICATE OF TRANSMISSION/MAILING

Express Mail Label: EV 529 865 418 US and EV 529 865 404 US			
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Signature	<i>William Carr</i>		
Typed or printed name	William Carr	Date	October 20, 2005



Effective on 12/08/2004.  
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

# FEE TRANSMITTAL

## For FY 2005

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$180.00)

### Complete if Known

Application Number	09/730,329
Filing Date	December 4, 2000
First Named Inventor	John
Examiner Name	Kam, C.
Art Unit	1653
Attorney Docket No.	015270-006460US

### METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): \_\_\_\_\_  
☒ Deposit Account Deposit Account Number: 20-1430 Deposit Account Name: Townsend and Townsend and Crew LLP

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee  
☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☒ Credit any overpayments

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### FEE CALCULATION

#### 1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Small Entity	Fee (\$)	Small Entity	Fee (\$)	Small Entity	Fee (\$)	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

#### 2. EXCESS CLAIM FEES

Fee Description	Small Entity	
	Fee (\$)	Fee (\$)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

<u>Total Claims</u>	<u>Extra Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>	<u>Multiple Dependent Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
_____ - 20 or HP = _____	x _____	\$ _____	= \$0	_____	_____	_____

HP = highest number of total claims paid for, if greater than 20

<u>Indep. Claims</u>	<u>Extra Claims</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
_____ - 3 or HP = _____	x _____	\$ _____	= \$0

HP = highest number of independent claims paid for, if greater than 3

#### 3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

<u>Total Sheets</u>	<u>Extra Sheets</u>	<u>Number of each additional 50 or fraction thereof</u>	<u>Fee (\$)</u>	<u>Fee Paid (\$)</u>
_____ - 100 = _____	/ 50 = _____	(round up to a whole number) x _____	= _____	

#### 4. OTHER FEE(S)

Non-English Specification, \$130 fee (no small entity discount)

Other: Information Disclosure Statement (after office action)

Fees Paid (\$)

180.00

#### SUBMITTED BY

Signature	<i>Mark G. Sandbaken</i>	Registration No. 39,354 (Attorney/Agent)	Telephone (650) 326-2400
Name (Print/Type)	Mark G. Sandbaken, Ph.D.		Date October 20, 2005

"Express Mail" Label No. EV 529865418 US, EV 529865404 US  
Date of Deposit October 20, 2005

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

By: 

William Carr

PATENT  
Attorney Docket No.: 015270-006460US  
Client Reference No.: 228-US-NEW4



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Varghese John et al.

Application No.: 09/730,329

Filed: December 4, 2000

For: BETA-SECRETASE ENZYME  
COMPOSITIONS AND METHODS

Examiner: C. Kam

Art Unit: 1653

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The references cited on the attached PTO/SB/08A and PTO/SB/08B forms are being called to the attention of the Examiner. Copies of the references [in compliance with the requirements of 1287 OG 163] are enclosed. It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Applicant also cites commonly owned copending applications directed to related subject matter:

08/480,498 filed 06/07/1995 issued as 5,744,346 on 04/28/1998

08/659,984 filed 06/07/1996 issued as 5,942,400 on 08/24/1999

08/660,531 filed 06/07/1996 issued as 6,221,645 on 04/24/2001

09/054,334 filed 04/02/1999 issued as 6,329,163 on 12/11/2001  
09/404,578 filed 09/23/1999 issued as 6,852,482 on 02/08/2005  
09/471,669 filed 12/24/1999  
09/723,722 filed 11/28/2000  
09/724,566 filed 11/28/2000 issued as 6,627,739 on 09/30/2003  
09/724,571 filed 11/28/2000 issue fee paid on 05/19/2005  
09/724,568 filed 11/28/2000  
09/724,569 filed 11/28/2000  
10/778,675 filed 02/12/2004  
11/069,377 filed 02/28/2005  
11/089,918 filed 03/25/2005  
11/090,399 filed 03/25/2005  
11/090,872 filed 03/25/2005

Applicant further cites the following commonly owned abandoned applications directed to related subject matter:

08/485,152 filed 06/07/1995  
60/114,408 filed 12/31/1998  
60/119,571 filed 02/10/1999  
60/139,172 filed 06/15/1999  
09/501,708 filed 02/10/2000  
09/723,739 filed 11/28/2000  
10/099,922 filed 03/15/2002

Applicants understand the Examiner can access papers from the prosecution of the cited cases electronically via PALM. However, if the Examiner has difficulty obtaining papers from that source he or she is invited to call the undersigned who will be happy to supply them.

As provided for by 37 CFR 1.97(g) and (h), no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information, and no inference should be made that the information and references cited are, or are considered to be material to patentability because they are in this statement. No inference should be made that the information and references cited are prior art merely because they are in this statement.

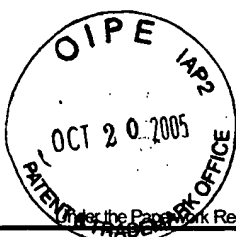
This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance. Please charge the IDS fee of \$180 to Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Mark G. Sandbaken, Ph.D.  
Reg. No. 39,354

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, Eighth Floor  
San Francisco, California 94111-3834  
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MGS:crf



PTO/SB/08A (10-01)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 11

### Complete if Known

Application Number	09/730,329
Filing Date	12/04/2000
First Named Inventor	John
Art Unit	1653
Examiner Name	Kam, C.
Attorney Docket Number	015270-006460US

### U.S. PATENT DOCUMENTS

Examiner	Cite No. <sup>1</sup>	Document Number Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	153	6,852,482	02-08-2005	Gurney et al.	
	149	6,844,148	01-18-2005	Gurney et al.	
	148	6,835,565	12-28-2004	Gurney et al.	
	91 B2	6,828,117	12-07-2004	Gurney et al.	
	139	6,825,023	11-30-2004	Gurney et al.	
	113	6,797,487	09-28-2004	Gurney et al.	
	114	6,790,610	09-14-2004	Gurney et al.	
	115	6,753,163	06-22-2004	Gurney et al.	
	116	6,737,510	05-18-2004	Gurney et al.	
	117	6,727,074	04-27-2004	Gurney et al.	
	118	6,706,485	03-16-2004	Gurney et al.	
	119	6,699,671	03-02-2004	Gurney et al.	
	154	6,627,739	09-30-2003	Anderson	
	120	6,500,667	12-31-2002	Gurney et al.	
	121	6,440,698	08-27-2002	Gurney et al.	
	122	6,420,534	07-16-2002	Gurney et al.	
	1	6,361,975	03-26-2002	Christie et al.	
	2	6,358,725	03-19-2002	Christie et al.	
	138	6,329,163	12-11-2001	Anderson et al.	
	3	6,319,489	11-20-2001	Powell et al.	
	4	6,319,689	11-20-2001	Powell et al.	
	5	6,313,268	11-06-2001	Hook	
	6	6,245,884	06-12-2001	Hook	
	7	6,245,964	06-12-2001	McConlogue et al.	
	8	6,221,645	04-24-2001	Chrysler et al.	

Examiner  
Signature

Date  
Considered

<sup>1</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>2</sup> Applicant's unique citation designation number (optional). <sup>3</sup> Kind Codes of U.S. Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>4</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>5</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>6</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>7</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231 60597020

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 2 of 11

**Complete if Known**

Application Number 09/730,329

Filing Date 12/04/2000

First Named Inventor John

Art Unit 1653

Examiner Name Kam, C.

Attorney Docket Number 015270-006460US

**U.S. PATENT DOCUMENTS**

Examiner	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code <sup>2</sup> (if known)			
	9	6,211,428	04-03-2001	Singh et al.	
	10	6,162,630	12-19-2000	Powell et al.	
	11	6,025,180	02-15-2000	Powell et al.	
	13	5,877,015	03-02-1999	Hardy et al.	
	141	5,863,756	01-26-1999	Barr et al.	
	14	5,849,560	12-15-1998	Abraham	
	15	5,837,672	11-17-1998	Schenk et al.	
	16	5,795,963	08-18-1998	Mullan	
	17	5,766,846	06-16-1998	Schlossmacher et al.	
	18	5,750,349	05-12-1998	Suzuki et al.	
	19	5,744,346	04-28-1998	Chrysler et al.	
	20	5,733,768	03-31-1998	Dixon et al.	
	21	5,593,846	01-14-1997	Schenk et al.	
	22	5,455,169	10-03-1995	Mullan	
	23	5,424,205	06-13-1995	Dovey et al.	
	140	2004/0234976	11-25-2004	Gurney et al.	
	123	2004/0166507	08-26-2004	Gurney et al.	
	124	2004/0048303	03-11-2004	Gurney et al.	
	125	2004/0043408	03-04-2004	Gurney et al.	
	128	2002/0081634	06-27-2002	Gurney et al.	
	130	2002/0037315	03-28-2002	Gurney et al.	
	131	2001/0021391	09-13-2001	Gurney et al.	
	142	10/817,979		Gurney et al.	
	143	10/477,076		Gurney et al.	
	144	09/668,314		Gurney et al.	
	94	09/548,370		Gurney et al.	
	97	09/548,369		Gurney et al.	

Examiner  
SignatureDate  
Considered

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<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Kind Codes of U.S. Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231  
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 3 of 11

**Complete if Known**

Application Number	09/730,329
Filing Date	12/04/2000
First Named Inventor	John
Art Unit	1653
Examiner Name	Kam, C.
Attorney Docket Number	015270-006460US

**U.S. PATENT DOCUMENTS**

Examiner	Cite No. <sup>1</sup>	Document Number Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	95	09/548,365		Gurney et al	
	27	09/404,133		Gurney et al.	
	28	09/277,229		Citron et al.	
	29	60/210,292		Hong et al.	
	30	60/178,368		Lin et al.	
	31	60/177,836		Lin et al.	
	152	60/169,232		Gurney et al.	
	32	60/168,060		Lin et al.	
	33	60/155,493		Gurney et al.	
	34	60/141,363		Lin et al.	
	35	60/139,172		Anderson et al.	
	36	60/119,571		Basi et al.	
	37	60/114,408		Basi et al.	
	38	60/101,594		Gurney et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Country Code <sup>3</sup>	Foreign Patent Document Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	170	EP	1 445 263	A1	08-11-2004			
	171	EP	855 442	A2	07-29-1998			
	39	EP	855 444	A2	07-29-1998			
	40	EP	848 062	A2	06-17-1998			
	166	GB	2 364 059	B	01-14-2004			
	167	GB	2 389 114	B	02-04-2004			
	168	GB	2 389 113	B	02-04-2004			
	169	GB	2 389 182	B	02-04-2004			
	134	WO	01/50829	A2	07-19-2001			

Examiner  
SignatureDate  
Considered

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 4 of 11

**Complete if Known**

Application Number	09/730,329
Filing Date	12/04/2000
First Named Inventor	John
Art Unit	1653
Examiner Name	Kam, C.
Attorney Docket Number	015270-006460US

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Country Code <sup>2</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	135	WO	01/49098	A2	07-12-2001			
	136	WO	01/49097	A2	07-12-2001			
	48	WO	01/38487	A2	05-31-2001			
	49	WO	01/36600	A1	05-25-2001			
	50	WO	01/31054	A1	05-03-2001			
	51	WO	01/29563	A1	04-26-2001			
	137	WO	01/23533	A2	04-05-2001			
	52	WO	01/00665	A2	01-04-2001			
	53	WO	01/00663	A2	01-04-2001			
	47	WO	00/69262	A1	11-23-2000			
	46	WO	00/68266	A1	11-16-2000			
	45	WO	00/58479	A1	10-05-2000			
	44	WO	00/56871	A2	09-28-2000			
	43	WO	00/47618	A3	08-17-2000			
	42	WO	00/23576	A2	04-27-2000			
	41	WO	00/17369	A2	03-30-2000			
	54	WO	99/64587	A1	12-16-1999			
	55	WO	99/46281	A2	09-16-1999			
	57	WO	99/34004	A2	08-07-1999			
	59	WO	99/31236	A2	06-24-1999			
	145	WO	98/37226	A1	08-27-1998			
	60	WO	98/26059		06-18-1998			
	188	WO	98/22597	A2	05-28-1998			
	61	WO	98/21589		05-22-1998			
	62	WO	98/13488		04-02-1998			
	63	WO	98/11236		03-19-1998			
	103	WO	97/47314		12-18-1997			
Examiner Signature					Date Considered			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Kind Codes of U.S. Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231  
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PTO/SB/08A (10-01)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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STATEMENT BY APPLICANT**

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Sheet 5 of 11

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Application Number	09/730,329
Filing Date	12/04/2000
First Named Inventor	John
Art Unit	1653
Examiner Name	Kam, C.
Attorney Docket Number	015270-006460US

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Country Code <sup>3</sup>	Foreign Patent Document Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>5</sup>
	56	WO	96/40885	A2	12-19-1996			
	58	WO	96/31122	A1	10-10-1996			
	102	WO	96/20725	A2	07-11-1996			

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	104	BALDWIN et al., "Crystal structures of native and inhibited forms of human cathepsin D: Implications for lysosomal targeting and drug design," <u>PNAS</u> , 90:6796-6800 (1993).	
	181	BORK, P., "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle," <u>Genome Research</u> , 10:398-400 (2000).	
	179	BROUN et al., "Catalytic Plasticity of Fatty Acid Modification Enzymes Underlying Chemical Diversity," <u>Science</u> , 282:131-133 (1998).	
	105	BROWN et al., "Evaluation of Cathepsins D and G and EC 3.4.24.15 as Candidate $\beta$ -Secretase Proteases Using Peptide and Amyloid Precursor Protein Substrates," <u>Journal of Neurochemistry</u> , 66:2436-2445 (1996).	
	106	CHEVALLIER et al., "Cathepsin D displays in vitro $\beta$ -secretase-like specificity," <u>Brain Research</u> , 750:11-19 (1997).	
	64	CHYUNG et al., "Novel $\beta$ -Secretase Cleavage of $\beta$ -Amyloid Precursor Protein in the Endoplasmic Reticulum/Intermediate Compartment of NT2N Cells," <u>Journal of Cell Biology</u> , 138:671-680 (1997).	
	178	DAS et al., "Estrogenic responses in estrogen receptor- $\alpha$ deficient mice reveal a distinct estrogen signaling pathway," <u>PNAS</u> , 94:12786-12791 (1997).	
	151	Declaration of Michael Bienkowski, Ph.D. in U.S. patent application 09/548,368	
	183	DENNIS et al., "Kunitz Domain Inhibitors of Tissue Factor-Factor VIIa," <u>J. Biol. Chem.</u> , 269(35):22129-22136 (1994).	
	107	DIEDRICH et al., "Nucleotide sequence of a cDNA encoding mouse cathepsin D," <u>Nucleic Acids Research</u> , 18:7184 (1990).	
	65	Elan Corporation, plc and Pharmacia Corporation announce research collaboration, News 08/09/2000, www.elancorp.com.	
	155	Examination Report for United Kingdom Application 00121314.9 dated November 1, 2002.	

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	156	Examination Report for United Kingdom Application 00121314.9 dated July 21, 2003.	
	157	Examination Report for United Kingdom Application 00121314.9 dated October 30, 2003.	
	158	Examination Report for United Kingdom Application 0318112.0 dated November 19, 2003.	
	159	Search and Examination Report for United Kingdom Application 0318112.0 dated September 24, 2003.	
	160	Search and Examination Report for United Kingdom Application 0318107.0 dated September 25, 2003.	
	161	Search and Examination Report for United Kingdom Application 0318113.8 dated September 25, 2003.	
	162	Examination Report for United Kingdom Application 0318113.8 dated November 19, 2003.	
	163	Examination Report for European Application 00919298.0 dated October 30, 2003.	
	164	Search Report for European Application 04006991.6 dated June 11, 2004.	
	165	Examination Report for New Zealand Application 534876 dated August 27, 2004.	
	146	Examination Report for European Application 00919298.0 dated September 20, 2004.	
	184	International Preliminary Examination Report for PCT application PCT/US00/03819 dated 9/4/02.	
	66	EVIN et al., "Alzheimer's disease amyloid precursor protein ( $\beta$ APP): proteolytic processing, secretases and $\beta$ A4 amyloid production," <u>Amyloid; Int. J. Exp. Clin. Invest.</u> 1:263-280 (1994).	

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	67	HAASS et al., "Amyloid $\beta$ -peptide is Produced by Cultured Cells During Normal Metabolism," <u>Nature</u> , 359:322-325 (1992).	
	68	HAASS et al., "The Swedish Mutation Causes Early-Onset Alzheimer's Disease by $\beta$ -Secretase Cleavage Within the Secretory Pathway," <u>Nature Medicine</u> , 12:1291-1296 (1995).	
	69	HAASS et al., " $\beta$ -Amyloid Peptide and 3-kDa Fragment are Derived by Distinct Cellular Mechanisms," <u>Journal of Biochemistry</u> , 268:3021-3024 (1993).	
	147	HARDY, J., "Framing beta-amyloid," <u>Nature Genetics</u> , 1(4):233-234 (1992).	
	70	HIROSAWA et al., "Characterization of cDNA Clones Selected by the GeneMark Analysis from Size-Fractionated cDNA Libraries From Human Brain," <u>DNA Res.</u> , 6(5):329-336 (1999).	
	71	HUSSAIN et al., "Identification of a Novel Aspartic Protease (Asp 2) as $\beta$ -Secretase," <u>Molecular and Cellular Neuroscience</u> , 14:419-427 (1999).	
	176	JACKSON et al., "The p47 <sup>phox</sup> Mouse Knock-Out Model of Chronic Granulomatous Disease," <u>J. Exp. Med.</u> , 182:751-758 (1995).	
	72	KANG et al., "The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor," <u>Nature</u> , 325:733-736 (1987).	
	182	KICK et al., "Structure-based design and combinatorial chemistry yield low nanomolar inhibitors of cathepsin D," <u>Chem. &amp; Biol.</u> , 4:297-307 (1997).	
	73	KITAGUCHI et al., "Novel Precursor of Alzheimer's Disease Amyloid Protein Shows Protease Inhibitory Activity," <u>Nature</u> , 331:530-532 (1988).	
	74	KNOPS et al., "Cell-type and Amyloid Precursor Protein-type Specific Inhibition of A $\beta$ Release by Bafilomycin A1, a Selective Inhibitor of Vacuolar ATPases," <u>Journal of Biological Chemistry</u> , 270:2419-2422 (1995).	
	75	KOO et al., "Evidence that Production and Release of Amyloid $\beta$ -Protein Involves the Endocytic Pathway," <u>Journal of Biological Chemistry</u> , 269:17386-17389 (1994).	

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	173	KRISTIE, T. M., "The Mouse Homologue of the Human Transcription Factor C1 (Host Cell Factor)," <u>J. Biol. Chem.</u> , 272(42):26749-26755 (1997).	
	187	KUNTZ, I. D., "Structure-Based Strategies for Drug Design and Discovery," <u>Science</u> , 257:1078-1082 (1992).	
	174	LI et al., "Cloning and Characterization of Three New Murine Genes Encoding Short Homologues of RNase P RNA*," <u>J. Biol. Chem.</u> , 270(42):25281-25285 (1995).	
	108	MAJER et al., "Structure-based subsite specificity mapping of human cathepsin D using statine-based inhibitors," <u>Protein Science</u> , 6:1458-1466 (1997).	
	76	MULLAN et al., "A Pathogenic Mutation for Probable Alzheimer's Disease in the APP Gene at the N-Terminus of $\beta$ -Amyloid," <u>Nature Genetics</u> , 1: 345-347 (1992).	
	150	Office Action dated 5/6/02 in U.S. patent application 09/548,368	
	77	PCT Search report for PCT/US99/20881	
	78	PCT Search report for PCT/US00/03819	
	79	PONTE et al., "A New A4 Amyloid mRNA Contains a Domain Homologous to Serine Proteinase Inhibitors," <u>Nature</u> , 331:525-527 (1988).	
	177	RAABE et al., "Knockout of the abetalipoproteinemia gene in mice: Reduced lipoprotein secretion in heterozygotes and embryonic lethality in homozygotes," <u>PNAS</u> , 95:8686-8691 (1998).	
	109	SAFTIG et al., "Amyloidogenic Processing of Human Amyloid Precursor Protein in Hippocampal Neurons Devoid of Cathepsin D," <u>Journal of Biological Chemistry</u> , 271:27241-27244 (1996).	
	110	SCHECHTER et al., "On the size of the active site in proteases. I. Papain," <u>Biochemical and Biophysical Research Communications</u> , 27:157-162 (1967).	
	80	SEUBERT et al., "Secretion of $\beta$ -amyloid Precursor Protein Cleaved at the Amino Terminus of the $\beta$ -amyloid Peptide," <u>Nature</u> , 361:260-263 (1993).	

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	81	SINHA et al., "Purification and Cloning of Amyloid Precursor Protein $\beta$ -Secretase from Human Brain," <u>Nature</u> , 402:537-540 (1999).	
	172	SUN et al., "Gene Structure, Chromosomal Localization, and Expression of the Murine Homologue of Human Proteinase Inhibitor 6 (PI-6) Suggests Divergence of PI-6 from the Ovalbumin Serpins*," <u>J. Biol. Chem.</u> , 270(27): 16089-16096 (1995).	
	82	SZECSI, "The Aspartic Proteases," <u>Scand. J. Clin. Lab. Invest.</u> , 52 (suppl. 210): 5-22 (1992).	
	185	TANG et al., "Evolution in the Structure and Function of Aspartic Proteases," <u>J. Cellular Biochem.</u> , 33:53-63 (1987).	
	83	TANZI et al., "Protease Inhibitor Domain Encoded by an Amyloid Protein Precursor mRNA Associated with Alzheimer's Disease," <u>Nature</u> , 331:528-530 (1988).	
	93	THOMPSON et al., "Expression and characterization of human $\beta$ -Secretase from candidates metalloendopeptidase MP78 and cathepsin D in $\beta$ APP-overexpressing cells," <u>Molecular Brain Research</u> , 48(2):206-214 (1997).	
	175	UMANS et al., "Targeted Inactivation of the Mouse $\alpha_2$ -Macroglobulin Gene*," <u>J. Biol. Chem.</u> , 270(34):19778-19785 (1995).	
	180	VAN DE LOO et al., "An oleate 12-hydroxylase from <i>Ricinus communis</i> L. is a fatty acyl desaturase homolog," <u>PNBS</u> , 92:6743-6747 (1995).	
	84	VASSER et al., " $\beta$ -secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," <u>Science</u> , 286(5440):735-741 (1999).	
	186	VISWANADHAN et al., "An Approach to Rapid Estimation of Relative Binding Affinities of Enzyme Inhibitors: Application to Peptidomimetic Inhibitors of the Human Immunodeficiency Virus Type 1 Protease," <u>J. Med. Chem.</u> , 39:705-712 (1996).	
	85	YAN et al., "Membrane-anchored Aspartyl Protease with Alzheimer's Disease $\beta$ -Secretase Activity," <u>Nature</u> , 402:533-537 (1999).	

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	101	YOUNG et al., "HIV-1 Protease Inhibitors Based on Hydroxyethylene Dipeptide Isosteres: An Investigation into the Role of the P <sub>1</sub> Side Chain on Structure-Activity," <u>J. Med. Chem.</u> , 35:1702-1709 (1992).	
	86	ZHAO et al., "β-Secretase Processing of the β-Amyloid Precursor Protein in Transgenic Mice Is Efficient in Neurons but Inefficient in Astrocytes," <u>Journal of Biological Chemistry</u> , 271:31407-31411 (1996).	

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